

AD _____

GRANT NO. DAMD17-95-1-5014

TITLE: Core Funding of the Medical Follow-Up Agency

PRINCIPAL INVESTIGATOR(S): William F. Page, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences
Washington, DC 20418

REPORT DATE: December 1995

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited.

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

19960220 001

DTIC QUALITY INSPECTED 1

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.				
1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE December 1995	3. REPORT TYPE AND DATES COVERED Final (18 Nov 94 - 31 Dec 95)	
4. TITLE AND SUBTITLE Core Funding of the Medical Follow-Up Agency			5. FUNDING NUMBERS DAMD17-95-1-5014	
6. AUTHOR(S) William F. Page, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) National Academy of Sciences Washington, DC 20418			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick Frederick, Maryland 21702-5012			10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) The principal purpose of providing core funding of the Medical Follow-up Agency (MFUA) is to put it in a more favorable position when it is called on to provide advice on issues of interest to the government. Continued core support will ensure that MFUA, as a part of the Academy carrying out its principal responsibility under its congressional charter, continues to provide scientifically rigorous and, therefore, credible advice to the government in a timely fashion. The specific uses of core support discussed in the report are three: develop new program areas, maintain and update important files and records resources, and modernize existing computer operations.				
14. SUBJECT TERMS epidemiology, follow-up studies			15. NUMBER OF PAGES 9	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

GENERAL INSTRUCTIONS FOR COMPLETING SF 298

The Report Documentation Page (RDP) is used in announcing and cataloging reports. It is important that this information be consistent with the rest of the report, particularly the cover and title page. Instructions for filling in each block of the form follow. It is important to *stay within the lines* to meet optical scanning requirements.

Block 1. Agency Use Only (Leave blank).

Block 2. Report Date. Full publication date including day, month, and year, if available (e.g. 1 Jan 88). Must cite at least the year.

Block 3. Type of Report and Dates Covered. State whether report is interim, final, etc. If applicable, enter inclusive report dates (e.g. 10 Jun 87 - 30 Jun 88).

Block 4. Title and Subtitle. A title is taken from the part of the report that provides the most meaningful and complete information. When a report is prepared in more than one volume, repeat the primary title, add volume number, and include subtitle for the specific volume. On classified documents enter the title classification in parentheses.

Block 5. Funding Numbers. To include contract and grant numbers; may include program element number(s), project number(s), task number(s), and work unit number(s). Use the following labels:

C - Contract	PR - Project
G - Grant	TA - Task
PE - Program Element	WU - Work Unit Accession No.

Block 6. Author(s). Name(s) of person(s) responsible for writing the report, performing the research, or credited with the content of the report. If editor or compiler, this should follow the name(s).

Block 7. Performing Organization Name(s) and Address(es). Self-explanatory.

Block 8. Performing Organization Report Number. Enter the unique alphanumeric report number(s) assigned by the organization performing the report.

Block 9. Sponsoring/Monitoring Agency Name(s) and Address(es). Self-explanatory.

Block 10. Sponsoring/Monitoring Agency Report Number. (If known)

Block 11. Supplementary Notes. Enter information not included elsewhere such as: Prepared in cooperation with...; Trans. of...; To be published in.... When a report is revised, include a statement whether the new report supersedes or supplements the older report.

Block 12a. Distribution/Availability Statement. Denotes public availability or limitations. Cite any availability to the public. Enter additional limitations or special markings in all capitals (e.g. NOFORN, REL, ITAR).

DOD - See DA 6290.24, "Distribution Statements on Technical Documents."

DOC - See authorities.

NASA - See Handbook NHB 2200.2.

NTIS - Leave blank.

Block 12b. Distribution Code.

DOD - Leave blank.

DOC - Enter DOE distribution categories from the Standard Distribution for Unclassified Scientific and Technical Reports.

NASA - Leave blank.

NTIS - Leave blank.

Block 13. Abstract. Include a brief (Maximum 200 words) factual summary of the most significant information contained in the report.

Block 14. Subject Terms. Keywords or phrases identifying major subjects in the report.

Block 15. Number of Pages. Enter the total number of pages.

Block 16. Price Code. Enter appropriate price code (NTIS only).

Blocks 17 - 19. Security Classifications. Self-explanatory. Enter U.S. Security Classification in accordance with U.S. Security Regulations (i.e., UNCLASSIFIED). If form contains classified information, stamp classification on the top and bottom of the page.

Block 20. Limitation of Abstract. This block must be completed to assign a limitation to the abstract. Enter either UI (unlimited) or SAR (same as report). An entry in this block is necessary if the abstract is to be limited. If blank, the abstract is assumed to be unlimited.

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the US Army.

Where copyrighted material is quoted, permission has been obtained to use such material.

Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

W. J. P. R. 12/14/95
PI - Signature Date

Table of Contents

Introduction	page 2
Body	page 3
Conclusions	page 6

INTRODUCTION

Purpose of Medical Follow-up Agency (MFUA) Core Funding

The principal purpose of providing core funding to MFUA is to put it in a more favorable position when it is called on to provide advice on issues of interest to the government. Continued core support will ensure that MFUA, as a part of the Academy carrying out its principal responsibility under its congressional charter, continues to provide scientifically rigorous and, therefore, credible advice to the government in a timely fashion.

History of MFUA Core Funding

In September 1988, the Office of Technology Assessment at the request of Senators Cranston and Murkowski of the Committee on Veterans' Affairs, convened a conference to discuss the Medical Follow-up Agency's (MFUA) future prospects and financial support. The report of that conference recommended that modest core support be provided MFUA. Subsequently, the Departments of the Army and of Veterans Affairs (VA), as well as the National Institutes of Health have provided core funding to MFUA.

Uses of MFUA Core Funding

The Medical Follow-up Agency was established in 1946 to facilitate the use of federal records, chiefly those of the armed forces and the VA, for medical research. Over the subsequent years, MFUA has served as a records and statistical resource, collaborating with qualified researchers to obtain the information they require from the records and participating in the analysis of the data.

In pursuing this general objective, continued core funding will help ensure that particular problems of importance and relevancy to the government are quickly identified; support the development of an annual program of studies designed to address such problems; and provide partial support for the MFUA director and essential staff to administer the MFUA oversight board. A necessary component in MFUA's continued development is the availability of core funding to develop new program areas, maintain and update important files and records resources, and modernize existing computer operations. Each of these tasks is discussed in the body of this report.

BODY

The three basic areas of MFUA core funding use are first discussed in detail. After these areas are each described, the results of core funding efforts are presented.

Develop New Program Areas

Much of the current work involves the utilization of MFUA records resources which have been concentrated, for the most part, in the WW II era. Because a great deal of research on the health of veterans necessarily focuses upon veterans of armed conflict--their range and intensity of wartime experiences are seldom duplicated in a peacetime environment--MFUA has traditionally concentrated on studies of WW II veterans, whose number and range of experiences are unique. As part of its continued growth, however, MFUA must expand its program into subsequent eras, where there are substantial new opportunities for research.

Accordingly, a priority of MFUA is the identification of new study areas. A major effort in support of this activity is to continue to create a catalog of the extensive MFUA collection of veteran cohorts with service-related disease conditions or putative exposures, and the distribution of the catalog, indexed by disease and exposure, to epidemiologists inside and outside of the federal government who are interested in veteran studies.

Maintain and Update Important Files and Records Resources; Pilot Work

MFUA has obtained access to and utilized a large number of records resources in the course of its work. MFUA's interest in these resources has led, in many cases, to the Agency's obtaining copies of valuable files and indices. As an example, the index to Army hospital admissions in WW II was a punch card file scheduled to have been destroyed some twenty years ago. MFUA obtained the funding to copy this index onto magnetic tape, and sent these tapes to the Army, keeping copies for itself. Subsequent interest in reconstructing military records on the part of the National Archives and Records Administration led to the "discovery" of this Army file and to press releases and newspaper coverage announcing the importance of the "new" resource. The sad fact is that, until this "discovery", the file had lain unused and unknown outside the Agency. Core funds provide the money to secure and examine and test indices such as the Army service number-Social Security Number index file.

A certain amount of pilot work is a critical component of almost all new studies because they often propose new uses for existing records. One of the crucial uses of continued core funds would be to underwrite pilot work for potential new studies suggested by investigators in core funding agencies and elsewhere. Without ongoing core funds, there is no satisfactory way to fund this kind of work.

Modernize Existing Computer Operations

MFUA's work is heavily dependent upon data files and computers, and its existing computer operations have evolved over the years to depend on the use of desktop computers linked together and to a large file server. MFUA is making a concentrated effort to reorganize and streamline, and "downsize" its computer operations. MFUA currently has a 5,000 reel tape library where most of our records resources are maintained. This tape repository is at the heart of the computer operation and must be copied to a DAT format and recataloged.

Results

During the period from 18 November 1994 through 17 November 1995, a number of program development activities have taken place. First, the Board of the Medical Follow-up Agency, which provides general oversight and direction, met in Washington, DC on 1 and 2 June 1995 at the National Academy of Sciences Foundry Building to review the MFUA program. At both meetings, specific discussion of new program activities were held with attendees from VA, DoD, HHS, and staff of the House and Senate Veterans Affairs Committees present for these discussions, and a number of areas for potential study were identified.

The proposed cohort catalog, an important dissemination activity was also discussed at the June Board meeting. Program initiation funds have been obtained from the National Academy of Sciences to initiate this project, which will need to be completed using core funds. A computer programmer has been hired to begin work to assemble the catalog, a detailed list of the extensive MFUA collection of veteran cohorts with service-related disease conditions or putative exposures, indexed by disease and exposure. When completed, it will be distributed to epidemiologists inside and outside of the federal government who are interested in veteran studies.

A 1991 National Cancer Institute workshop concluded that the title, "The Emerging Epidemic of Non-Hodgkin's Lymphoma" accurately describes the world-wide situation. The increased risk of cancer recurrence following perioperative transfusion has been well described and has been attributed to transfusion-associated immune suppression. Immune suppression—genetic or acquired—results in much greater risk for non-Hodgkin's lymphoma, other lymphomas, and malignancies; but this fact does not rule out a blood-borne etiologic agent. In all studies of this type, the illness requiring transfusion complicates the reasoning process, and what is needed is a study of patients transfused solely for the management of trauma. MFUA has begun to conduct a pilot and feasibility study with 2,021 battle injured individuals, 516 of whom were transfused, and approximately 1500 controls to assess methods and gather preliminary morbidity and mortality data. The battle injured cohort was assembled by a Navy surgical research team at Danang Hospital in Vietnam in 1968 as part of a larger

study of transfusion practices and has been provided to MFUA by a collaborator at the Naval Health Research Center, San Diego. Cause-specific morbidity and mortality endpoints will be sought from automated Department of Defense and Department of Veterans Affairs (VA) hospitalization discharge diagnosis databases, the VA Beneficiary Identification and Record Locator System, VA death benefit claims folders, and possibly the National Death Index. Data collection will be passive; no contact with study subjects is planned.

The second pilot study has been completed and concerns the long-term effects of hepatitis C infection. Underlying this study is a unique collection of sera left over from U.S. Army funded studies of streptococcal disease and rheumatic fever in recruits at Fort Francis E. Warren, Wyoming, during the period 1949 to 1954. Of some 23,00 individuals in the original studies, only active duty participants with adequate identifier information and at least one good serum specimen left over and now stored in freezers at the University of Minnesota, are in the cohort. These 9,500 recruits will be screened for antibody to hepatitis C. Those found infected with hepatitis C, along with controls, will be followed-up for cause-specific mortality endpoints, especially chronic cirrhosis and hepatocellular carcinoma. These healthy young men will serve well as surrogates for the hundreds of thousands of healthy blood donors found each year to be chronically infected with hepatitis C, a disease whose natural history is unknown at this time.

CONCLUSIONS

Core funding has contributed substantially to MFUA efforts in the past year. Core funds have supported program development, file maintenance, and computer modernization efforts. These same kinds of activities, however, will require continued support.

MFUA plans to continue to hold meetings of its Board twice a year, and core funds are necessary to support these gatherings. These meetings will not only provide oversight from the Board, but also allow MFUA collaborators to meet with the Board and discuss current and planned projects. The interaction of Board members and MFUA collaborators provides one of the single best means to generate ideas for new studies and thus to develop a stronger MFUA program. Work will likewise continue on the production and dissemination of the cohort catalog.

MFUA needs to continue to maintain its files. Future efforts must be concentrated in reprogramming the existing software systems, copying to DAT format and checking our extensive data tape library, and indexing the new databases. This is a personnel-intensive effort that cannot be associated with any given project; thus, continued core funding is required. The improvements afforded by these changes, however, will substantially benefit all MFUA projects.

MFUA will also continue to conduct pilot studies of the long-term effects of transfusion and of hepatitis C infection. There may be additional pilot studies as well, for example, an examination of the feasibility of creating a new twin registry.

Finally, core funds will enable continued modernization of MFUA computers. Although the existing workstations are sufficiently powerful for current applications, it may be necessary to upgrade them and the MFUA file server if additional disk space becomes necessary. Also personal computers in MFUA's St. Louis office may need to be upgraded in the near future to take advantage of more hardware intensive software.